

<b>PRE-APPEAL BRIEF REQUEST FOR REVIEW</b>		Docket Number (Optional) <b>02508.0110-00000</b>
<p>I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]</p> <p>on _____</p> <p>Signature _____</p> <p>Typed or printed name _____</p>		<p>Application Number <b>10/591,233</b></p> <p>Filed <b>May 7, 2007</b></p> <p>First Named Inventor <b>Malin ERNEBRANT et al.</b></p> <p>Art Unit <b>1616</b></p> <p>Examiner <b>Abigail L. FISHER</b></p>

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).

Note: No more than five (5) pages may be provided.

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| <input type="checkbox"/> applicant/inventor.<br>_____<br><i>//Aaron L. Parker//</i>  | Signature             |
| <input type="checkbox"/> assignee of record of the entire interest.<br>See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.<br>_____<br><i>Aaron L. Parker</i> | Typed or printed name |
| <input checked="" type="checkbox"/> attorney or agent of record.<br>Registration number <u>50,785</u><br>_____<br><i>202.408.4000</i>                                  | Telephone number      |
| <input type="checkbox"/> attorney or agent acting under 37 CFR 1.34.<br>Registration number if acting under 37 CFR 1.34 _____<br>_____<br><i>July 22, 2011</i>         | Date                  |

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below\*.

\*Total of \_\_\_\_\_ forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Applicant requests a pre-appeal brief panel review of the rejections set forth in the Final Office Action dated March 22, 2011 (“Final Office Action”) and Advisory Action dated June 13, 2011 (“Advisory Action”). This request is being filed concurrently with a Notice of Appeal under 37 C.F.R. § 41.31, the appropriate fee, and a completed form PTO/SB/33. No amendments are being filed with this Request.

In the Final Office Action, the Office rejects claims 1-7, 11-14, 16-17, 20 and 24 under 35 U.S.C. § 103(a) as unpatentable over “Zander” (U.S. Patent No. 5,296,242, to Zander) in view of “Duponchelle” (U.S. Patent No. 6,309,673, to Duponchelle). (Final Office Action at page 3.) Applicant respectfully disagrees and traverses this rejection for the following reasons.

The Examiner contends that based on Zander and Duponchelle, “it would have been obvious . . . to manipulate the pH of the starting materials to achieve the desired final pH,” and “to produce a more stable bicarbonate solution that does not need the use of special equipment to keep the carbon dioxide concentration constant while maintaining the partial pressure of the carbon dioxide to that . . . of the same magnitude as the atmosphere.” (Final Office Action at 15-16; Advisory Action at 2.) Applicant respectfully disagrees.

The Examiner’s basis for finding a *prima facie* case of obviousness is premised on mischaracterizations of Zander and a failure to completely consider all elements of the present claims. Moreover, even if one of ordinary skill in the art would have been motivated to combine Zander and Duponchelle, as proposed by the Examiner, the teachings of Zander and Duponchelle conflict with each other, providing no motivation for their combination. As a result, Zander’s and Duponchelle’s conflicted teachings fail to provide any reasonable expectation that combining their teachings would successfully lead to the claimed medical solutions. As such, the Examiner fails to establish a *prima facie* case of obviousness.

Claim 1 recites, *inter alia*, a first single solution comprising bicarbonate and carbonate **in such proportions that a partial pressure of carbon dioxide in the first single solution is of the same order of magnitude as a partial pressure of carbon dioxide in the atmosphere**, and has a pH of 10.1 - 10.5.” (emphasis added.) The as-filed specification teaches that it is the particular proportion of bicarbonate/carbonate

in the first single solution that allows it to be in equilibrium with the partial pressure of carbon dioxide in the atmosphere, and therefore maintain a stable pH. (As-filed Specification at page 3.) In order for the first single solution to be in equilibrium with the partial pressure of carbon dioxide in the atmosphere, **there must be a greater concentration of carbonate than bicarbonate in the first single solution.** (See e.g., Examples 1-40 in the as-filed specification.)

In contrast, Zander teaches a bicarbonate alkaline solution comprising 19.1 mmol alkali bicarbonate and 6.1 mmol alkali carbonate, i.e., **greater concentration of bicarbonate than carbonate.** (Zander at Abstract.) It is this particular “bicarbonate concentration” and the “CO<sub>2</sub> partial pressure correspond[ing] to the physiological blood plasma values,” that allow Zander’s dialysis solutions to eliminate incorrect dosing and the incidence of alkalosis or acidosis. (Zander at col. 2, ll. 35-55.) Zander’s alkaline solutions comprising a greater concentration of bicarbonate than carbonate teach away from the claimed alkaline solutions “comprising bicarbonate and carbonate in such proportions that a partial pressure of carbon dioxide . . . is of the same order of magnitude as a partial pressure of carbon dioxide in the atmosphere” (i.e., having a greater concentration of carbonate than bicarbonate in the first single solution). In view of Zander, therefore, one of ordinary skill would have been led away from the presently claimed medical solutions. However, the Examiner argues that “Zander recognizes the desire to have the magnitude of the carbon dioxide of the solution **match that of the atmosphere.** Therefore, manipulation to achieve this matching would have been obvious.” (Advisory Action at 2.) The Examiner further states that “Zander teaches liquids which have a carbon dioxide partial pressure **which corresponds to that of atmospheric air** do not change their overall carbon dioxide content which makes them more stable.” (*Id.*) (emphasis added). The Examiner’s statements have no basis. Nowhere does Zander teach or suggest an alkaline solution having a partial pressure of carbon dioxide of the solution that matches that of the **atmosphere**, and instead expressly teaches that its dialysis solutions have “CO<sub>2</sub> partial pressure correspond[ing] to the **physiological blood plasma values.**” (Zander at col. 2, ll. 35-55.) (emphasis added). One of ordinary skill in the art would understand that there is a significant difference in partial pressure of carbon dioxide in the **atmosphere**, as recited in the

present claims, versus partial pressure of carbon dioxide in **blood plasma**, as taught in Zander. Thus, the Examiner's contention that "Zander would be expected to have the same stability as instantly claimed," is baseless, and nowhere supported by Zander. Applicant respectfully points out that "[i]f the examiner is relying on personal knowledge to support the finding of what is known in the art, the examiner *must* provide an affidavit or declaration setting forth specific factual statements and explanation to support the finding. (See 37 CFR 1.104(d)(2)." M.P.E.P. § 2144.03(C) (emphasis added)).

As discussed in the previous Response, neither Zander nor Duponchelle recognize that it is the proportion of bicarbonate/carbonate in the first single solution that allows the solution to have the same magnitude of partial pressure of carbon dioxide as that of the atmosphere. However, the Examiner contends that "the claims do not require any specific proportions." (Advisory Action at 2.) This is also incorrect. Claim 1 recites, *inter alia*, "a first single solution comprising bicarbonate and carbonate in such proportions that a partial pressure of carbon dioxide in the first single solution is of the same order as a partial pressure of carbon dioxide in the atmosphere." (emphasis added). The Examiner improperly disregards this element of claim 1. (*In re Wilson*, 424 F.2d. 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) ("[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art.")) . Thus, the Examiner must still show that all of the elements of the claims are taught in the prior art in order to arrive at the present invention. Yet, neither Zander nor Duponchelle teach or suggest the specific proportion of carbonate/bicarbonate necessary to equilibrate with the carbon dioxide in the atmosphere in order to obtain a first single solution and an overall medical solution having a stable pH.

Moreover, the conflicted teaches of Zander and Duponchelle discourage their combination. As the Federal Circuit stated in *Karsten Manufacturing Corp. v. Cleveland Golf Co.*, 242 F.3d, 1376, 1385, 58 U.S.P.Q.2d 1286, 1293 (Fed. Cir. 2001), "conflicting teachings cannot be viewed as suggesting their combination." (See M.P.E.P. § 2143.01(II)) The U.S. Patent and Trademark Office's 2010 KSR Guidelines Update 75 Fed. Reg. 53643, 53647 (Sept. 1, 2010) ("Guidelines") explains:

An inference that a claimed combination would not have been obvious is especially strong where the prior art's teachings **undermine** the very reason being proffered as to

why a person of ordinary skill would have combined the known elements.

(Guidelines at 53659 (discussing *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314 (Fed. Cir. 2009))) (emphasis added). Not only does Duponchelle teach away from Zander (e.g., teaches that the high pH of the acidic solution of Zander is too high and Zander's organic acids "will enhance the formation of glucose degradation products, which in turn may damage the peritoneal membrane"), Duponchelle also teaches that it is "preferable to have **all buffer available as bicarbonate.**" (Duponchelle at col. 3, ll. 42-58.) (emphasis added). Thus, Duponchelle teaches away from Zander, and the claimed medical solutions, which include both bicarbonate and carbonate in a particular proportion. Therefore, the conflicting teachings of Duponchelle and Zander undermine the Examiner's proposed combination; one of ordinary skill in the art would not have even looked to Duponchelle to modify Zander.

As a result of Duponchelle's and Zander's conflicted teachings, one of ordinary skill in the art would not have had a reasonable expectation that their combination would successfully lead to the claimed medical solutions. According to M.P.E.P. 2144.05, "[a] particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation." Here, the Examiner's argument is based on the faulty premise that manipulation of the proportion of bicarbonate/carbonate to match the partial pressure of carbon dioxide in the atmosphere is a property that a skilled artisan would have generally recognized as a variable that should be considered in preparing medical compositions. However, as discussed above, neither Zander nor Duponchelle recognize that it is the proportion of bicarbonate/carbonate in the first single solution that allows it to have the same magnitude of partial pressure of carbon dioxide as that of the atmosphere. In addition to their conflicted teachings, the combination of Zander and Duponchelle fail to lead one of ordinary skill in the art to the presently claimed medical solutions.

As demonstrated in the Declaration under 37 C.F.R. §1.132 of co-inventor Malin Ernebrant ("Declaration") submitted in the Response dated January 21, 2011, the stability of a bicarbonate solution containing an approximate 1:6 ratio of carbonate to

bicarbonate resulted in a stable pH over a period of 17 days. (Declaration at page 3, Table 4.) Thus, the Examiner's statement that "Applicants have not demonstrated the criticality of the pH of the initial solutions," is incorrect. It is the criticality of the proportion of carbonate/bicarbonate that allows the first single solution to be in equilibrium with the partial pressure of carbon dioxide in the atmosphere which subsequently allows the pH of the first single solution and overall medical solution to be stable over time. Evidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness. (M.P.E.P. § 716.02(a)(II)). Accordingly, this evidence is relevant to the issue of obviousness and must be considered. M.P.E.P. 2141(II).

The Examiner also rejects claims 8-10, 15, 18-19, 21-23, 25 and 29-33 under 35 U.S.C. § 103(a) as unpatentable over Zander in view of Duponchelle and further in view of "Linden" (International Patent Application No. WO 01/89478 to Linden et al.). (Final Office Action at page 10.) The Examiner concedes that Zander fails to teach "the addition of a third or fourth single solution," and "does not specify that the sterilization is heat sterilization at a temperature of at least 100°C," and relies on Linden to remedy these deficiencies. (See *id.*) However, Linden fails to remedy the deficiencies of Zander and Duponchelle discussed above. Thus, the combination of Zander, Duponchelle and Linden fails to render instant claims 8-10, 15, 18-19, 21-23, 25 and 29-33 obvious, and Applicant respectfully requests withdrawal of this rejection.

In view of the foregoing remarks, Applicant respectfully requests reconsideration of the current rejections and timely allowance of all pending claims. Please grant any extensions of time required to enter this paper and charge any additional required fees to Deposit Account No. 06-0916.